

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re application of: **Ruben *et al.***

Application Serial No.: 09/774,639

Art Unit: 1634

Filed: February 1, 2001

Examiner: Myers, C.

For: Secreted Protein HBJFE12
(as amended)

Attorney Docket No.: PZ013P1C1

Commissioner for Patents
Washington, D.C. 20231

Declaration of Dr. George Komatsoulis Under 37 C.F.R. § 1.132

I, George Komatsoulis, do hereby declare and say:

1. I am a citizen of the United States, residing at 9518 Garwood Street, Silver Spring, MD, 20901.

2. Since February 3, 1997, I have served as a scientist of Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, Maryland 20850, assignee of the captioned application.

3. I have personal knowledge that the expression of the polynucleotide of SEQ ID NO:43 was assessed in hundreds of human tissues, including cancerous tissue (*e.g.*, B-cell lymphoma tissue), as well as many other "normal" (*i.e.*, non-cancerous) blood cells (*e.g.*, T cells, B cells, monocytes). Based on this assessment, no expression was observed in "normal" blood cells. In contrast, expression was observed in B-cell lymphoma tissue.

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

United States code and that such willful false statements may jeopardize the validity of the application of any patents issued thereupon.

George A. Komatsoulis
Dr. George Komatsoulis

10 Jan - 2003
Date



\$Nucleotide

Boo

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AUTHORS Worley, K.C.
 TITLE Direct Submission
 JOURNAL Submitted (16-SEP-1998) Human Genome Sequencing Center, Department of Molecular and Human Genetics, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA
 COMMENT On Aug 8, 1998 this sequence version replaced gi:3298526. Sequencing is completed to a minimum standard of double strand coverage with a minimum of 2 clones and 2 reads with no ambiguities or 2 chemistries with a minimum of 2 clones and 3 reads with no ambiguities. If the sequence quality does not meet this standard, it will be indicated in the annotation.

The repeat regions shown were identified using RepeatMasker by Adrian Smit.

Sequence similarities were identified using Powerblast by Jinghui Zhang.

Exon/Intron boundaries of identified genes were chosen if there were canonical splice junctions that maintained sequence continuity across the splice junctions.

FEATURES	Location/Qualifiers
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<u>repeat_region</u>	complement(6595..6890) /rpt_family="AluSg"
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BASE COUNT 36381 a 20956 c 19880 g 31662 t

ORIGIN

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(Roswell Park Cancer Institute Human PAC library) complete sequence.
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Plus Strand HSPs:

Score = 3170 (481.7 bits), Expect = 3.3e-143, Sum P(2) = 3.3e-143
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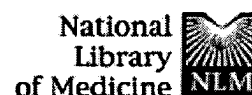
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Loss of genetic material from the short arm of chromosome 12 is a frequent secondary abnormality in non-Hodgkin's lymphoma.

Jonveaux P, Le Coniat M, Derre J, Vecchione D, Berger R.

Unite INSERM U 301, Institut de Genetique Moleculaire, Paris, France.

Abnormalities of the short arm of chromosome 12 have been detected in a wide variety of hematopoietic disorders. Seven cases of non-Hodgkin's lymphoma (NHL) are reported with various rearrangements involving bands 12p13 or 12p11, associated with other chromosome changes. A review of the literature confirms that rearrangements of 12p, mainly at band 12p13, are nonrandom chromosomal abnormalities in all subtypes of NHL, as in other malignant blood disorders. No common translocation could, however, be detected, and 12p abnormalities may be considered as secondary chromosomal events. Most of the 12p rearrangements involving translocation of genetic material of unknown origin, suggest that they result in loss of 12p segment.

PMID: 2050601 [PubMed - indexed for MEDLINE]

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FISH identifies different types of duplications with 12q13-15 as the commonly involved segment in B-cell lymphoproliferative malignancies characterized by partial trisomy 12.

Dierlamm J, Wlodarska I, Michaux L, Vermeesch JR, Meeus P, Stul M, Criel A, Verhoef G, Thomas J, Delannoy A, Louwagie A, Cassiman JJ, Mecucci C, Hagemeijer A, Van den Berghe H.

Center for Human Genetics, University of Leuven, Belgium.

Clinical, cytogenetic, fluorescence in situ hybridization (FISH), and Southern blot data of 18 patients with different subtypes of B-cell non-Hodgkin's lymphoma, cytogenetically characterized by partial trisomy 12, are presented. These chromosomal changes occurred predominantly in clinically progressive chronic lymphocytic leukemia, mixed cell type, and advanced-stage follicle center cell lymphoma at the time of relapse or transformation into diffuse large cell lymphoma. Partial trisomy 12 consistently included the long arm of chromosome 12, either completely or partially, and resulted from dup(12q) or other rearrangements involving chromosome 12. The duplications were cytogenetically identified as dup(12)(q13q23), dup(12)(q13q22), or dup(12)(q13q15) in follicle center cell lymphoma or t(14;18)-positive diffuse large cell lymphoma; dup(12)(q13q22) or dup(12)(q13q24) in chronic lymphocytic leukemia; and dup(12)(q13q21) in a case of t(14;18)-negative diffuse large cell lymphoma. FISH, using library probes and a panel of YAC probes, mapped along the long arm of chromosome 12, confirmed the cytogenetic results in all cases analyzed except for three cases of t(14;18)-positive follicle center lymphoma or diffuse large cell lymphoma with dup(12q). In these cases, FISH showed similar, possibly identical, duplications, which involved a region more centromeric (12q11-21) than assumed by karyotypic analysis (12q13-22 or 12q13-23) and included alphoid DNA sequences, a combination hitherto unknown. In addition, commonly duplicated regions of chromosome 12 could be defined: 12q11-21, including alphoid DNA sequences for follicle center cell lymphoma or t(14;18)-positive diffuse large cell lymphoma, 12q13-22 for chronic lymphocytic leukemia, and 12p13-q15 for marginal zone cell lymphoma, all of which overlapped in 12q13-15. Whether these regions, especially 12q13-15, may contain genes which are important in

malignant transformation or disease progression of B-cell
lymphoproliferative malignancies characterized by complete or partial
trisomy 12 remains to be determined.

PMID: 9331566 [PubMed - indexed for MEDLINE]

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